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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,168	03/04/2002	Duncan H. Hunter	UWA-001.01 (23433-101)	9927

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FOLEY HOAG, LLP
PATENT GROUP, WORLD TRADE CENTER WEST
155 SEAPORT BLVD
BOSTON, MA 02110

EXAMINER

HARTLEY, MICHAEL G

ART UNIT

PAPER NUMBER

1616

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/091,168

Applicant(s)

HUNTER ET AL.

Examiner

Michael G. Hartley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 and 16-22 is/are rejected.
- 7) ☒ Claim(s) 15 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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Response to Amendment

The amendment filed 2/9/2004 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6, 8-12 and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reed (US 5,746,997).

Reed discloses precursor compounds of formula 5 in column 5. This formula can easily be substituted by embodiments in the disclosure in column 5-6 to encompass the precursor compounds of the instant claims. For example, Reed teaches that any of the R1 substituents can be an alkyl chain of up to 10 carbons, and the higher chain alkyls (e.g., 10 carbons) would be within the scope of a "polymer" and insoluble polymer, given its broadest reasonable interpretation, see also column 3 for definition of R1. Thus, one R1 would be a polymer and the other two R1 groups attached to the Sn would correspond to the R3-Sn-R3 group as claimed. The aryl is within the scope of aryl as claimed, see claim 1, which defines aryl in the formula to be naphthalene, pyridine, etc., which are polycyclic or heterocyclic aryls. The Z-ODP (Z=C(O)NH-) groups corresponds to the instant formula wherein Y is C(O)NH-R4 and R4 is oligonucleotide or -side, see columns 2-3. Also, Reed clearly discloses that the linkers Y and Y' may be absent. Substituting the formula 5 as disclosed by Reed, as set forth above, would yield a compound that is within the scope of the instant claims. Also, see claim 1 formula (iii) of Reed, wherein such compounds are claimed as are the process of preparing such compounds. The kits claims are not distinguished from Reed, in that, they only contain the polymer, which is contained in compositions by Reed and written instructions, which are not patentably relevant, as these are written materials and are related to an

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intended use. Also, the term "kit" is in the preamble and does not add any further limitations to the composition.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Reed (US 5,746,997) as applied to claims 1-6, 8-12 and 16-19 above, and further in view of Wilbur Wilbur (US 5,609,848).

Reed fails to disclose that the Sn-substitution may be for proteins or peptides, as well as, nucleotides.

Wilbur teaches that methods involving Sn-substitution of aryl compounds, similar to those disclosed by Hunter, may be employed for proteins to provide the advantage of yielding diagnostic or therapeutic agents having high specific activity, see abstract and columns 1-2.

It would have been obvious to one of ordinary skill in the art to use precursor compounds and methods disclosed by Reed to also radiolabel proteins or peptides because it is known in the art that analogous Sn-precursor compounds and Sn substitution methods can be used for radiolabeling compounds having other biomolecules (e.g., proteins or peptides) to provide the advantage of obtaining various site-specific radiopharmaceuticals, as shown by Wilbur.

Claims 1-14 and 16-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter (WO 99/18053) in view of Reed (US 5,746,997) and Wilbur (US 5,609,848).

Hunter discloses polymer precursor compounds having the formula shown on page 4. The compounds on page 4 are similar to those claimed. For example, the second compound on page 4 is similar to the claimed formula when L is the first formula possible therefore, R is aryl and alkylamino. The only difference is that Hunter does not disclose that the aryl group may be a polycyclic or heterocyclic aryl as now claimed. The first formula on page 4 is also similar to various claims, note that R₂ can be carbonyl group, thus relating to claims 3-4. Also R₁ and R₂ can be various alkyl groups, as claimed. The polymer is an insoluble polymer, such as, polystyrene, which may be reacted with divinylbenzene to yield compounds of claim 15, see pages 8-9. The compounds may be in kit formulation and include various components therefor, filtration devices, etc., e.g., page 2. The compounds are prepared by methods as

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claimed, i.e., using a support (the polymer) for the radiolabeling procedure, etc., see pages 7-9 and the examples.

Hunter fails to disclose that the aryl group in the precursor compounds and methods is a polycyclic or heterocyclic aryl group. Hunter also fails to specifically teach the precursor compounds for labeling compounds substituted with peptides, proteins, nucleosides or nucleotides, (yielding, *inter alia*, benzamides), as claimed.

However, it is well known in the art that analogous Sn-precursor compounds and methods may substitute benzene, polycyclic and heterocyclic aryls, as equivalent aryl groups, at the same position that corresponds to R as claimed and the benzene of Hunter.

Reed discloses precursor compounds that are analogous to those disclosed by Hunter and are for the same purpose. Reed teaches that the aryl group may be a benzyl (benzoic acid, see abstract), a heterocyclic or polycyclic aryl as equivalents, see claim 1. Reed also teaches that Sn-substitution using Sn-derivatized precursor compounds are known to be useful for labeling oligonucleotides with radioiodine to provide the advantage of yielding site-specific diagnostic agents, see abstract and columns 1-2.

Wilbur also teaches that equivalence of benzene to polycyclic or heterocyclic aryls in analogous precursor compounds, see column 3. In fact, Wilbur specifically teaches such equivalence by stating "The nature of the aromatic ring is not critical and may be mono-, bi, tri or higher number of rings...The aromatic rings may consist of all carbon atom or may contain heteroatoms" see column 3. Wilbur teaches that methods involving Sn-substitution of aryl compounds, similar to those disclosed by Hunter, may be employed for proteins to provide the advantage of yielding diagnostic or therapeutic agents having high specific activity, see abstract and columns 1-2.

The main difference between the claims and Hunter is that the precursor compounds of Hunter have benzene as the R group, while the instant claims have been limited to the R group being a polycyclic aryl or heteroaryl. Hunter provides an improved method of preparing haloaromatic compounds, which use a polymer support for improved means of radiolabeling various compounds using Sn-substitution. Hunter fails to specifically disclose that the benzene group may be a polycyclic or heterocyclic group, but does teach that the improved methods may be employed to "any number of

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radiolabeled haloaromatic compounds" on page 23. The prior art clearly teaches that processes for preparing haloaromatic compounds that the aryl group may be either benzene or a polycyclic or heteroaryl group, interchangeably, as an equivalent, to provide various radiolabeled haloaromatic compounds, as shown by Reed and Wilbur.

It would have been obvious to one of ordinary skill in the art to substitute the aryl (benzene) disclosed by Hunter in precursor compounds disclosed therein because Hunter teaches an improved polymer support methods that can be employed for various radiopharmaceuticals and because it is well known in the art that analogous precursor compounds may have a polycyclic or heterocyclic aryls as an equivalent to a benzene in the compounds of Hunter to provide the advantage of obtaining various haloaromatic (polycyclic or heteroaryl) radiolabeled compounds, as shown by Reed and Wilbur.

Further, it would have been obvious to one of ordinary skill in the art to employ the precursor compounds and methods disclosed by Hunter for various compounds, including those having targeting agents, such as, proteins, nucleosides, etc., because Hunter teaches that the improved precursor compounds and methods may be used for various radiopharmaceuticals and it is known in the art that analogous Sn-precursor compounds and Sn substitution methods can be used for radiolabeling compounds which have proteins, nucleotides, etc., to provide the advantage of obtaining site-specific radiopharmaceuticals, as shown by Reed and Wilbur.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Omum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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Claims 16 and 17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,461,585 in view of Reed (US 5,746,997) and Wilbur (US 5,609,848).

The claims of '585 patent are drawn to a method that is very similar to that claimed. For example, when L is the first possibility, R is aryl and Y=R2, the patented claims only differ in the aryl moiety.

However, as stated above, the use of benzene is a known equivalent to polycyclic or heteroaryls at this position in analogous methods and provides the advantage of providing a wider range of radiopharmaceuticals, namely, radiohalogenated polycyclic or heteroatom aromatic compounds, as shown by Reed and Wilbur. It would have been obvious to one of ordinary skill in the art to employ the methods of the '585 patent to polycyclic or heteroaryl compounds because it is well known in the art that analogous Sn-substitutions methods can employ such compounds as equivalents to those used in the '585 patent, as shown by Reed and Wilbur.

Response to Arguments

Applicant's arguments with respect to claims 1-20 have been considered but are moot in view of the new ground(s) of rejection, set forth above.

Applicant's arguments filed 2/9/2004 have been fully considered but they are not persuasive.

Applicant asserts that Hunter does not disclose the steps in methods claims 20-22 and that the secondary references do not supply the missing elements.

This is not found persuasive because Hunter teaches an improved process of preparing radiolabeled compounds that may be employed for various radiohalogenated compounds. Hunter teaches that the improved method uses a solid support (a polymer) for radiolabeling. Reed and Wilbur teach analogous methods for providing various biomolecule-containing radiopharmaceuticals. The radiopharmaceuticals methods disclosed by both Reed and Wilbur teach that it is well known in the art to use a benzoic acid, reacted with an amine to form a benzamide, as these are the precursors used in the methods of Reed and Wilbur, see Reed columns 7-8 and claims 10+ and Wilbur columns 5-6 that teach an aryl group with a carboxylic acid, and the use of iodobenzoic acid, with an amine group of protein to

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form the radiolabeled protein which is a benzamide. The methods to radiolabel the nucleoside and proteins disclosed by Reed and Wilbur provide all the steps in the claims, excluding the use of a solid support, which is disclosed by Hunter.

Allowable Subject Matter

Claim 15 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The prior art fails to provide the requisite motivation to arrive at the specific compounds set forth in claim 15 by modification to select specific groups that would arrive at these compounds.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

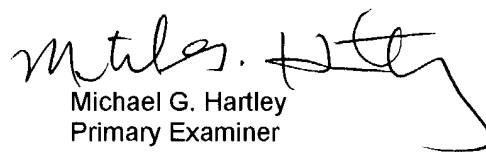
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Hartley whose telephone number is (571) 272-0616. The examiner can normally be reached on M-F, 7:30-5, off alternative Mondays.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Michael G. Hartley
Primary Examiner
Art Unit 1616

3/12/2004